Exhibit A-2

[redacted]

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (JLH) **DEMAND FOR JURY TRIAL**
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA, Defendant/Counter-Plaintiffs, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC., Plaintiff/Counter-Defendants.	[redacted]

PLAINTIFF'S CONCISE STATEMENT OF FACTS IN SUPPORT OF ITS MOTION FOR PARTIAL SUMMARY JUDGMENT NO. 1 REGARDING INVALIDITY OF CLAIM 1 OF U.S. PATENT NO. 9,994,851

Amanda S. Williamson (admitted *pro hac vice*)
Christopher J. Betti (admitted *pro hac* vice)
Krista V. Venegas (admitted *pro hac* vice)
Wan-Shon Lo (admitted *pro hac vice*)
Maria E. Doukas (admitted *pro hac vice*)
Zachary Miller (admitted *pro hac vice*)
Michael T. Sikora (admitted *pro hac vice*)
MORGAN, LEWIS & BOCKIUS LLP
110 N. Wacker Drive, Suite 2800
Chicago, IL 60601
Telephone: 312.324.1000 | Fax: 312.324.1001
amanda.williamson@morganlewis.com
christopher.betti@morganlewis.com
krista.venegas@morganlewis.com
shon.lo@morganlewis.com
maria.doukas@morganlewis.com
zachary.miller@morganlewis.com
michael.sikora@morganlewis.com

Amy M. Dudash (DE Bar No. 5741)
MORGAN, LEWIS & BOCKIUS LLP
1201 N. Market Street, Suite 2201
Wilmington, DE 19801
Telephone: 302.574.3000 | Fax: 302.574.3001
amy.dudash@morganlewis.com

Julie S. Goldemberg (admitted *pro hac vice*)
Alison P. Patitucci (admitted *pro hac vice*)
MORGAN, LEWIS & BOCKIUS LLP
2222 Market Street
Philadelphia, PA 19103
Telephone: 215.693.5000 | Fax: 215.963.5001
alison.patitucci@morganlewis.com

Attorneys for Plaintiff/Counterclaim Defendant Nippon Shinyaku Co., Ltd. and Counterclaim Defendant NS Pharma, Inc.

Dated: September 26, 2024

1. Sarepta asserts only claim 1 of U.S. Patent No. 9,994,851, which claims priority to PCT/AU2005/000943, filed June 28, 2005. *See* D.I. 536-2; D.I. 2-9, Ex. I ('851 patent) claim 1; Ex. 1 (priority application). The specific combination of limitations in claim 1 was not disclosed together in the priority application. *See id*. It was first added during prosecution of the '851 Patent in a preliminary amendment dated September 15, 2017. D.I. 428-1 (SRPT-VYDS-000) 3099-3100.

2. On May 9, 2024, this Court clarified that claim 1 of the '851 Patent "requires 100% complementarity to consecutive bases of a target region of exon 53 throughout the entire length of the antisense oligonucleotide." D.I. 573.

3. [redacted]. Ex. 2 (Hastings Suppl.) ¶44. [redacted]. *Id.*; *see also* Ex. 6 (Dowdy Suppl. Dep.) 298:5-301:1 (Sarepta's expert Dr. Dowdy admitting [redacted]). [redacted], Ex. 2 (Hastings Suppl.) ¶70, [redacted], *id.* ¶72.

4. [redacted]. *Id.* ¶45; Ex. 6 (Dowdy Suppl. Dep.) 282:5-11. [redacted]. Ex. 2 (Hastings Suppl.) ¶¶53, 55; Ex. 3 (Dowdy Suppl.) ¶43-49, 59. [redacted]. Ex. 2 (Hastings Suppl.) ¶60.

5. U[redacted]

[redacted] *Id.* ¶¶75-76. [redacted] *Id.* [redacted] . *Id.* ¶78; *see also id.* ¶80.

6. [redacted] Ex. 3 (Dowdy Suppl.) ¶¶33, 35. [redacted] *Id.* ¶36. [redacted] *Id.* ¶¶44-45.

7. [redacted] . Ex. 6 (Dowdy Suppl. Dep.) 312:11-313:6.

8. [redacted] *Id.* 314:2-315:17.

9. The specification describes experimental work for 212 AOs targeted to various exons of the human dystrophin pre-mRNA, but not a single tested AO falls within the scope of claim 1. D.I. 2-9, Ex. I ('851 Patent) 4:44-49, tbl. 1A; *see also id.* 4:56-61, tbl. 1C; Ex. 2 (Hastings Suppl.) ¶ 86; Ex. 3 (Dowdy Suppl.) ¶111 (Table 1).

10. The specification lists the exon 53-skipping results for 11 AOs, none of which fall within the claimed genus. D.I. 2-9, Ex. I ('851 Patent) at tbl. 39, 32:33-36.

11. The closest the specification gets to disclosing test results within the scope of claim 1 is SEQ ID NO. 195. D.I. 2-9, Ex. I ('851 Patent) tbl. 39; Ex. 5 (Dowdy Dep.) 188:10-15. But

SEQ ID NO. 195 has uracil bases, not the claimed thymine bases. D.I. 2-9, Ex. I ('851 Patent) Table 1A, Table 39; D.I. 427-2 (Dowdy Rebuttal) ¶ 109. It also is not a morpholino AO. Ex. 2 (Hastings Suppl.) ¶86. SEQ ID NO. 195 induced only "very faint skipping." D.I. 2-9, Ex. I ('851 Patent) Table 39. *see also* Ex. 2 (Hastings Suppl.) ¶ 86.

12. The specification **does not** disclose any test results for (1) a morpholino AO; (2) an AO with the claimed thymine bases; (3) an AO that induces exon 53 skipping that is 20, 22, 23, 26, 28, 29 or 30 bases in length; (4) an AO with nucleobase chemical modifications; or (4) an AO linked to a chemical moiety. Ex. 2 (Hastings Suppl.) ¶¶86-89.

13. [redacted] Ex. 2 (Hastings Suppl. ¶88); Ex. 6 (Dowdy Suppl. Dep.) 359:8-13. [redacted] Ex. 5 (Dowdy Dep.) 50:13-51:11; Ex. 2 (Hastings Suppl.) ¶¶ 88-89.

14. Sarepta contends NS's accused product VILTEPSO falls within the scope of claim 1. D.I. 89 ¶¶ 35-73. [redacted] D.I. 427-1 (Dowdy Opening) ¶¶ 138-139, 148; *see also* Ex. 7 (showing VILTEPSO on an edge of the genus).

15. [redacted] D.I. 427-3 (Dowdy Reply) ¶84. [redacted] D.I. 427-1 (Dowdy Opening) ¶¶128-134; *see also* Ex. 7 (showing VYONDYS 53 on an edge of the genus).

16. [redacted]. Ex. 2 (Hastings Suppl.) ¶60; *compare* Ex. 3 (Dowdy Suppl.) ¶16, n. 1-2 ([redacted]), *with* Ex. 6 (Dowdy Suppl. Dep.) 287:20-288:8. [redacted] D.I. 2-9, Ex. I ('851 Patent). [redacted]. Ex. 6 (Dowdy Suppl. Dep.) 317:18-318:8.

17. [redacted] Ex. 3 (Dowdy Suppl.) ¶62.

18. The specification does not use the term "hot spot," "hotspot" or "hot-spot," nor does it state that the region delineated by positions +23+69 in the human exon 53 pre-mRNA is a region amenable to exon skipping. *See* D.I. 2-9, Ex. I ('851 Patent); *see also* Ex. 6 (Dowdy Suppl. Dep.) 355:3-11.

19. [redacted] D.I. 427-3 (Dowdy Reply) ¶ 67.

20. These examples and results are provided without explanation as to whether and why AOs binding at or near the so-called "hot spot" induce exon 53 skipping. *See e.g.,* D.I. 2-9, Ex. I ('851 Patent) 64:32-65:67.

21. [redacted] Ex. 4 (Wood Reply) ¶¶30-35; Ex. 5 (Dowdy Dep.) 190:2-14 (discussing SEQ ID No. 193), 217:20-

218:20 (discussing [redacted]). [redacted] Ex. 2 (Hastings Suppl.) ¶172 & p. 101; Ex. 5 (Dowdy Dep.) 216:20-217:12

22. [redacted]

Ex. 5 (Dowdy Dep.) 44:11-15; Ex. 6 (Dowdy Suppl. Dep.) 259:17-260:8.

23. T[redacted]. *See* Ex. 6 (Dowdy Suppl. Dep.) 267:14-269:19-, 271:11-272:25 (admitting [redacted]).

24. [redacted] Ex. 6 (Dowdy Suppl. Dep.) 371:11-372:25.

25. [redacted] D.I. 313, Ex. 5 ¶¶ 68-86; Ex. 2 (Hastings Suppl.) ¶¶ 186-196; Ex. 5 (Dowdy Dep.) 192:1-4, 209:19-23.

26. As Sarepta argued during prosecution, "[t]here was a significant level of unpredictability . . . at the time of the invention." D.I. 428-1 (SRPT-VYDS-0002984) 4784. Sarepta relied on publications from 2002 and 2003 to argue that "interfering with exon selection for inclusion before splicing is 'a process that is not yet well understood'" and "that significant experimentation is required to arrive at specific oligonucleotides" because there was "no insight into the actual position of the targeted sequence within the completely folded RNA structure." *Id.* 4790-4792. Sarepta also described "examples of unpredictability [] reported … at or near the date of Applicants' invention." *Id.* 4792-4793. This unpredictability applied "even in situations where the antisense oligonucleotides are very similar to each other in terms of nucleotide sequence, and other variables concerning the chemical backbone are fixed." *Id.* at 4793.

27. Sarepta explained how the "recognition of the lack of predictability in the field of

exon skipping continued beyond 2005." *Id.* 4793-4794. Sarepta pointed to a 2007 publication that stated "there are still no clear rules to guide investigators in their design" and a 2009 publication noting that "in general a trial and error procedure is still involved to identify potent AONs." *Id.* Sarepta also relied on a 2011 publication that stated "selecting specific [AO] sequences to induce effective dystrophin exon skipping remains an unpredictable exercise." *Id.* 4794-4795.

28. Sarepta made similar arguments during the '007 Interference. Sarepta told the Patent Office that "many factors influence the binding of an AO[] to its target, including AO[] length, target accessibility, nucleobase sequence, modifications to the chemical backbone, Watson-Crick 'mismatches,' and modifications to the internucleotide linkages." D.I. 427-23 (UWA Motion 1) 4. "Consequently, there is tremendous variability and unpredictability in the efficacy of different AONs targeted to different regions of the dystrophin pre-mRNA, and each different AON needs to be empirically tested." *Id*.

> **When the competing applications in this interference were filed**, a handful of specific operative exon skipping antisense oligonucleotides ("AONs") targeting exon 53 had been discovered, **and the path to identifying others was largely unknown**. Both parties submitted broad generic claims in the hope that identification of broader families of operative AONs would follow predictably from those narrower discoveries. **Subsequent experience has revealed that operative sequences are actually highly unpredictable**, varying with parameters such as nucleobase sequence, length, backbone chemistry, and internucleotide linkages.

Id. at 1 (emphasis added).

29. As Sarepta argued during Interference '007, the need to test each and every potential AO to determine whether an AO falls within the scope of the claims (*i.e.*, whether it induces exon 53 skipping) is reflected in the specification. D.I. 427-24 (UWA Reply 1) 9 ("[T]he need to test each and every AON is also reflected in UWA's specification, which states that '[o]nce efficient exon skipping [has] been induced with one antisense molecule, subsequent overlapping antisense molecules may be synthesized and then evaluated.").

CERTIFICATE OF SERVICE

The undersigned certifies that on September 26, 2024, a copy of the foregoing, which was filed under seal, was served via electronic mail on the following counsel of record:

William B. Raich
Michael J. Flibbert
John M. Williamson
Yoonhee Kim
Yoonjin Lee
FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, LLP
901 New York Avenue, NW
Washington, DC 20001-4413
(202) 408-4000
william.raich@finnegan.com
michael.flibbert@finnegan.com
john.williamson@finnegan.com
yoonhee.kim@finnegan.com
yoonjin.lee@finnegan.com

Charles E. Lipsey
J. Derek McCorquindale
Ryan P. O'Quinn
L. Scott Burwell
1875 Explorer Street, Suite 800
Reston, VA 20190-6023
(571) 203-2700 charles.lipsey@finnegan.com
derek.mccorquindale@finnegan.com
ryan.o'quinn@finnegan.com
scott.burwell@finnegan.com

Alissa K. Lipton
Eric J. Lee, Ph.D.
Two Seaport Lane
Boston, MA 02210-2001
(617) 646-1600
alissa.lipton@finnegan.com
eric.lee@finnegan.com

Jack B. Blumenfeld
Megan E. Dellinger
MORRIS, NICHOLS, ARSHT & TUNNELL LLP
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899
(302) 658-9200
jblumenfeld@morrisnichols.com
mdellinger@morrisnichols.com

Amanda P. Reeves
Anna M. Rathbun
Graham B. Haviland
Jesse Aaron Vella
LATHAM & WATKINS LLP
555 Eleventh Street, NW, Suite 1000 Washington, D.C. 20004
(202) 637-2200
amanda.reeves@lw.com
anna.rathbun@lw.com
graham.haviland@lw.com

/s/ Amy M. Dudash
Amy M. Dudash (DE Bar No. 5741)